Remarks

Claims 1-40, 55 and 56 are pending in the subject application, with claims 1-29, 55 and 56 withdrawn from consideration. By this Amendment, applicant has cancelled claims 1-29, 32-34, 55 and 56 without disclaimer or prejudice to applicant's right to pursue the subject matter of these claims in the future. In addition, applicant has amended claims 30, 35, 37, 38 and 39, and added new claims 57 and 58. Support for the amendments to claim 30 may be found in the specification as originally filed at, *inter alia*, page 9, lines 12 to 22; page 9, line 36 to page 13, line 11; page 11, line 22 to page 12, line 19; page 16, lines 13-14; in Example 4 beginning on page 48; and in Example 5 beginning on page 54. Claim 35 has been amended to correct its dependency from claim 34 to claim 30. Support for the amendments to claim 37 may be found in the specification as originally filed at, *inter alia*, page 12, lines 18-25. Support for the amendments to claim 38 may be found in the specification as originally filed at, *inter alia*, page 12, line 27 to page 13, line 15; page 9, lines 3 to 22; in Example 4 beginning on page 48; and in Example 5 beginning on page 54. Support for the amendments to claim 39 may be found in the specification as originally filed at, *inter alia*, page 13, lines 16-17. Support for new claims 57 and 58 may be found in the specification as originally filed at, *inter alia*, page 9, lines 18-22; and page 49, lines 4-6. Applicant notes that new claims 57 and 58, depend from claims 30 and 38, respectively, which are part of Examiner's claim Group V, the elected invention.

Applicant maintains that the amendments to the claims raise no issue of new matter and respectfully request that these amendments be entered as stated on page 14 of applicant's response to the restriction.

Restriction Requirement

In the June 2, 2006 Office Action the Examiner stated on page 2 that applicant responded to the Restriction and/or Election of species *without* traverse. On page 3, the Examiner stated that applicant elected group V *with* traverse.

In response, applicant wishes to clarify that the election was made with traverse.

Claims Rejected Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 30-40 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the claimed invention.

The Examiner stated that claim 30 recites the limitation "the small molecule" in step (e) and that there is no antecedent basis for this limitation in the claim.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claim 30 to replace the term "the small molecule" with "the molecule". Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that, for claim 30, applicant must claim subject matter which she regards as her own invention. The Examiner indicated that the screening molecule recited in claim 1 does not correspond to the H_1-Y-H_2 molecules described in the specification and their methods of use in dimerization.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claim 30 to clarify the subject matter being claimed. In addition, applicants note that in the H_1-Y-H_2 molecule, "Y" may be present or absent, see page 5, lines 10-12 for example. The support for the claim amendments is detailed hereinabove. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection

The Examiner also stated that with regard to claim 30 the phrase "capable of selectively binding to and selectively forming a covalent bond with a receptor" is vague and indefinite because it is unclear whether the candidate molecule, substrate or entire molecule is capable of selectively binding to and selectively forming a covalent bond with a receptor.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claim 30 to clarify the invention. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

The Examiner also rejected claims 30 and 37 under 35 U.S.C. §112, second paragraph, as allegedly indefinite in that the term "small" recited therein is a relative term.

In response, applicant respectfully traverses the Examiner's rejection. Applicant notes that the term "small molecule" is routinely used and understood by those in the art. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claims 30 and 37 to remove the term objected to by the Examiner. Accordingly, applicant respectfully requests that the

Examiner reconsider and withdraw this ground of rejection.

The Examiner stated that claim 33 recites the phrase "the transcription activation domain", that claim 36 recites the phrase "the molecule", and that claim 38 recites the phrase "the candidate molecule", but that these terms do not have antecedent basis.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein canceled claim 33 without prejudice. Applicant notes that the recitation of the term "the molecule" in claim 36 has correct antecedent basis in claim 30, for example, see the preamble of claim 30. Applicant has hereinabove amended claim 38 to remove the term objected to by the Examiner. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

The Examiner rejected claim 38 under 35 U.S.C. §112, second paragraph, in that the phrase "providing a screening molecule having a ligand which has a specificity for the unknown target receptor" is allegedly vague and indefinite in that it is not clear how a person can provide a ligand that is specific for a receptor without knowing at least something about the receptor to which the ligand binds.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claim 38 to remove the phrase objected to by the Examiner. Applicant maintains that as amended, claim 38 fulfills the requirements of 5 U.S.C. §112, second paragraph. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 30-40 under 35 U.S.C. §112, first paragraph, as containing subject matter that, allegedly, is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, was in possession of the claimed invention.

Established Nature of Yeast 3-Hybrid System

Applicant initially notes that the current invention is an improvement on established 3-hybrid systems, with the identification of the advantages of a CID that covalently binds one of the fusion proteins so as to enhance the cut-off K_d of the whole system (see Background of the Invention and page 5, lines 24-27).

Applicant further notes that, as M.P.E.P. §2164.01 states, "a patent need not teach, and *preferably omits*, what is well known in the art." (emphasis added), citing In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); and Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987). M.P.E.P §2163(II)(a)(3) confirms that "what is conventional or *well known to one of ordinary skill in the art need not be disclosed in detail*" (emphasis added), again referring to Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d at 1384, 231 USPQ at 94.

As such, applicant notes that there are already issued patents in this field, for example U.S. Patent Nos. 5,928,868 (submitted with the Information Disclosure Statement filed November 10, 2003 in connection with the above-identified application and attached hereto as **Exhibit A**) and 7,083,918 (**Exhibit B**). The '868 patent, which was issued on July 27, 1999, before the priority date of

the current application, describes the yeast 3-hybrid system and is based the even earlier established 2-hybrid system. The patent describes fusion proteins, DNA-binding domains, reporter genes, chemical inducers of dimerization and transcriptional activators (e.g. see Background regarding the 2-hybrid system components; see Fig. 1, and Examples 2-6 regarding the 3-hybrid system).

Applicant maintains that the Examiner's assertions with regard to the written description of the current invention, especially in view of what those of skill in the art are aware of and what is already known, fail to take into account the established nature of the field.

Specific Points Raised by the Examiner

The Examiner stated, inter alia, that independent claim 30 fails to provide a definition, structure, formula or chemical name for any of the compounds recited in the claim, and that there is substantial variation within the genus claimed.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claim 30. As amended, claim 30 recites the nature of the first fusion protein, the second fusion protein including the receptor domain, and further states that the recited moiety is capable of selectively binding to and selectively forming a covalent bond with a receptor domain. Applicant further notes that the receptor domain is specifically defined as comprising a penicillin binding-protein or a thymidine synthase, and such information, in conjunction with the characteristic that the recited moiety is capable of selectively binding to and selectively forming a covalent bond with the receptor domain, clearly connotes definite structural information that one of skill in the art would recognize as describing the invention in accordance with 35 U.S.C. §112, first paragraph.

The Examiner rejected claims 30-40 under 35 U.S.C. §112, first paragraph, alleging that the specification, while being enabling for the cephem-Mtx induced dimerization of LexA-R61 to DHFR-B42, allegedly does not reasonably provide enablement for the use of any screening molecule with any set of fusion proteins.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claim 30, from which claims 31-37 depend, and has amended claim 38, from which claims 39 and 40 depend. Applicant notes that, as amended, independent claims 30 and 38 recite that the screening molecule comprises a moiety capable of selectively binding to and selectively forming a covalent bond with a receptor domain, that the first fusion protein comprises a LexA DNA-binding domain fused to a known target receptor domain against which the candidate molecule is screened, and that the second fusion protein comprises (i) a penicillin-binding-protein ("PBP") or a thymidine synthase ("TS") enzyme receptor domain capable of binding to and forming a covalent bond with the screening molecule and (ii) a B42 transcription activation domain. Applicant further notes that a working example is set forth in the specification (Example 4). Furthermore, applicant notes that Abida et al. cited by the Examiner, point out that different CIDs did not affect transcription activation levels to any great extent (see page 893, last paragraph in left hand column). Moreover, applicants note that examples of moieties capable of selectively binding to and selectively forming a covalent bond with a penicillin-binding-protein ("PBP") or a thymidine synthase receptor domain, e.g. cephem and fluorouracil, respectively, are set forth in the specification, e.g. at page 9, lines 18-22.

Accordingly, applicant maintains that claims 30 and 38 as amended

are enabled by the specification, and that one of skill in the art (and the Examiner has acknowledged that the skill level is high, and applicant has indicated the established nature of the field) would be able to make and use the claimed invention based on the disclosure. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

Claims Rejected Under 35 U.S.C. §102(b)

The Examiner rejected claims 30-40 under 35 U.S.C. §102(b), as allegedly anticipated by Lin et al. *J. Am. Chem. Soc.*, 2000, 122:4247-4248, as evidenced by Simons et al., *PNAS*, 1981, 78(6):3541-3545. The Examiner asserted, inter alia, that Lin et al. disclose a second fusion protein that comprises a receptor domain, namely a GR-B42.

In response, applicant respectfully traverses the Examiner's rejection. However, in order to expedite prosecution, and without conceding the correctness of the Examiner's position, applicant has herein amended claim 30, from which claims 31-37 depend, and has amended claim 38, from which claims 39 and 40 depend. As amended, independent claims 30 and 38 recite a second fusion protein which comprises (i) a receptor domain penicillin-binding-protein ("PBP") or a thymidine synthase ("TS") enzyme capable of binding to and *forming a covalent bond* with the screening molecule and (ii) a B42 transcription activation domain. This element is not taught in Lin et al., and thus applicant maintains that Lin et al. does not anticipate the claimed invention. Accordingly, applicant respectfully requests that the Examiner reconsider and withdraw this ground of rejection.

Double Patenting

The Examiner rejected claims 30-33 and 36-40 as provisionally

rejected under the judicially created doctrine of obviousness-type double patenting over claims 133, 135-137, 141-147 and 150-160 of U.S. Patent Application No. 10/705,644 as evidenced by Fan et al. (1989) *Proc. Int. Symp. Pteridines Folic Acid Deriv.*, 9th Meeting date 1989, 116-5.

In response, applicant respectfully traverses the Examiner's rejection. In addition, it is noted that the rejection is a provisional rejection, and, as such, applicant will consider filing a terminal disclaimer, if necessary, if this is the only remaining rejection.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicant's undersigned attorneys invites the Examiner to telephone them at the number provided below.

No fee, other than the enclosed $510.00 fee for a three-month extension of time, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

Gary J. Gershik

John P. White
Registration No. 28,678
Gary J. Gershik
Registration No. 39,992
Attorneys for Applicant
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Gary J. Gershik 12/4/06

Gary J. Gershik Date
Reg. No. 39,992